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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,971	11/26/2001	Markku Ahotupa	2630-113	8814

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,971	AHOTUPA ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *22* is/are allowed.

6)☒ Claim(s) *6, 21 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 6 and 21-23 are pending.

2. In view of the amendment filed 2/22/05, the following rejection remains.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 6, 21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,451,849 B1 (filed March 30, 1999) in view of Morikawa *et al* (J. Pharm Pharmacol 44(10): 859-61, Oct 1992; PTO 892).

The '849 patent teaches a method of administering to an individual an effective amount of lignan such as hydroxymatairesinol (See entire document, col. 2, in particular). The reference hydroxymatairesinol from plant is converted to enterolactone by gut microflora (See col. 2, lines 19- 20, in particular). The reference method is useful in inhibiting the over activity of cell such as a decrease in LDL oxidation (See col. 6, lines 27-30, Table 3, in particular), inhibition of lipid peroxidation (See col. 7, lines 4-5, Table 2, in particular) and superoxide anion scavenging (See col. 7, line 44, in particular). The '849 patent teaches hydroxymatairesinol is useful for treating cancers (See abstract, in particular). The '849 patent further teaches enterolactone is a metabolite

of hydroxymatairesinol and one can increases the level of enterolactone by administering to a person an effective amount of hydroxymatairesinol (see claim 5 of '849 patent, in particular).

The invention in claim 21 differs from the teachings of the reference only in that the method of inhibiting myeloperoxidase activity in neutrophils in an individual by administering to said individual an effective of enterolactone.

The invention in claim 6 differs from the teachings of the reference only in that the method of inhibiting myeloperoxidase activity in neutrophils in an individual by administering to said individual an effective of enterolactone wherein the myeloperoxidase activity in converting the reactive oxygen species, released by oxidative burst caused by stimulus of said neutrophils, is decreased.

The invention in claim 23 differs from the teachings of the reference only in that the method of inhibiting oxidative burst in neutrophil by administering to an individual an effective of hydroxymatairesinol.

Morikawa *et al* teach a method of inhibiting myeloperoxidase activity or oxidative burst in human neutrophils in vitro by administering enterolactone that inhibits fMLP induced myloperoxidase activity as measured by luminal-enhanced chemiluminescence (LCL) response or oxidative bursts by measuring superoxide production by human polymorphonuclear leukocytes (neutrophils) (See abstract, page 859, col. 2, results, Fig 1, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer enterolactone that inhibits myeloperoxidase activity or oxidative activity of neutrophils as taught by Morikawa et al for a method of inhibiting myeloperoxidase in neutrophils in an individual since enterolactone is a metabolite of hyroxymatairesinol as taught by the '849 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Morikawa *et al* teach enterolactone inhibits fMLP induced myeloperoxidase activity as measured by luminal-enhanced chemiluminescence (LCL) response or oxidative bursts by measuring superoxide production by human polymorphonuclear leukocytes (neutrophils) (See abstract, page 859, col. 2, results, Fig 1, in particular). The '849 patent teaches enterolactone is a metabolite of hydroxymatairesinol and one can increases the level of enterolactone by administering to a person an effective amount of hydroxymatairesinol (see claim 5 of '849 patent, in particular).

Hydroxymatairesinol is useful as an antioxidant useful for treating cancers (See abstract, in particular).

Applicants' arguments filed 2/22/05 have been fully considered but are not found persuasive.

Applicants' position is that claim 1 has been rewritten as new claim 21 and claim 6 has been amended. Claims 2-5 and 17-18 have been canceled. The '849 patent and Morikawa et al as combined fail to teach that hydroxymatairesinol is able to decrease the formation in vivo of reactive oxygen species, which in turn would cause lipid oxidation. The '849 patent discloses that hydroxymatairesinol is a useful anti-oxidant because it is an inhibitor of lipid peroxidation and LDL oxidation. Morikawa et al discloses that enterolactone inhibits fMLP produced oxidative burst in neutrophils. The references, as combined, fail to teach or suggest all the claim limitations of newly added claim 23. Nowhere in the references cited is there any motivation or a suggestion to inhibit oxidative burst or myeloperoxidase activity in neutrophils by administering hydroxymatairesinol.

In response, the '849 patent teaches administering hydroxymatairesinol to individual (See entire document, col. 2, in particular). The '849 patent further teaches enterolactone is a metabolite of hydroxymatairesinol where hydroxymatairesinol is converted to enterolactone by gut microflora (See col. 2, lines 19- 20, in particular); one can increases the level of enterolactone by administering to a person an effective amount of hydroxymatairesinol (see claim 5 of '849 patent, in particular). The claimed invention differs from the teachings of the reference only in that a method of inhibiting myeloperoxidase activity or oxidative burst in neutrophils by administering to an individual either enterolactone or hydroxymatairesinol.

Morikawa *et al* teach a method of inhibiting myeloperoxidase activity or oxidative burst in human neutrophils in vitro by administering enterolactone that inhibits fMLP induced myeloperoxidase activity as measured by luminal-enhanced chemiluminescence (LCL) response or oxidative bursts by measuring superoxide production by human polymorphonuclear leukocytes (neutrophils) (See abstract, page 859, col. 2, results, Fig 1, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer enterolactone that inhibits myeloperoxidase activity or oxidative activity of neutrophils as taught by Morikawa et al for a method of inhibiting myeloperoxidase in neutrophils in an individual since enterolactone is a metabolite of hyroxymatairesinol as taught by the '849 patent. From the combined teachings of the references,

it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Morikawa *et al* teach enterolactone inhibits fMLP induced myeloperoxidase activity as measured by luminal-enhanced chemiluminescence (LCL) response or oxidative bursts by measuring superoxide production by human polymorphonuclear leukocytes (neutrophils) (See abstract, page 859, col. 2, results, Fig 1, in particular). The '849 patent teaches enterolactone is a metabolite of hydroxymatairesinol and one can increases the level of enterolactone by administering to a person an effective amount of hydroxymatairesinol (see claim 5 of '849 patent, in particular). Hydroxymatairesinol is useful as an antioxidant useful for treating cancers (See abstract, in particular). The in vitro myeloperoxidase activity and myeloperoxidase activity of enterolactone as taught by Morikawa would obviously be the same as that of in vivo activity since most of the drug activity are investigated in vitro prior to in vivo. In fact, the specification on pages 8-9 discloses neutrophils from human are isolated and myeloperoxidase activity and oxidative burst were measured in vitro.

In response to applicants' argument that nowhere in the references cited is there any motivation or a suggestion to inhibit oxidative burst or myeloperoxidase activity in neutrophils by administering hydroxymatairesinol, the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose. Section MPEP 2144.07.

6. Claim 22 is allowed.

7. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

10. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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